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NOTICE OF ALLOWANCE AND FEE(S) DUE

50828

7590

03/31/2009

DAVID S. RESNICK
NIXON PEABODY LLP
100 SUMMER STREET
BOSTON, MA 02110-2131

EXAMINER

KAM, CHIH MIN

ART UNIT

PAPER NUMBER

1656

DATE MAILED: 03/31/2009

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/567,422 | 09/08/2006 | Boris Schwartzburd | 057878-000024 | 8394 |
| TITLE OF INVENTION: METHOD FOR THE PURIFICATION OF A NON-IMMUNOGLOBULIN PROTEIN COMPRISING AN IMMUNOGLOBULIN-LIKE (IG-LIKE) DOMAIN | | | | |

| APPLN. TYPE | SMALL ENTITY | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE |
|----------------|--------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | NO | \$1510 | \$300 | \$0 | \$1810 | 06/30/2009 |

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. **PROSECUTION ON THE MERITS IS CLOSED.** THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN **THREE MONTHS** FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. **THIS STATUTORY PERIOD CANNOT BE EXTENDED.** SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
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Alexandria, Virginia 22313-1450
or Fax **(571)-273-2885**

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

50828 7590 03/31/2009
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BOSTON, MA 02110-2131

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

| |
|--------------------|
| (Depositor's name) |
| (Signature) |
| (Date) |

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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10/567,422 09/08/2006 Boris Schwartzburd 057878-000024 8394

TITLE OF INVENTION: METHOD FOR THE PURIFICATION OF A NON-IMMUNOGLOBULIN PROTEIN COMPRISING AN IMMUNOGLOBULIN-LIKE (IG-LIKE) DOMAIN

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|----------------|--------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | NO | \$1510 | \$300 | \$0 | \$1810 | 06/30/2009 |

| EXAMINER | ART UNIT | CLASS-SUBCLASS |
|--------------|----------|----------------|
| KAM, CHH MIN | 1656 | 530-350000 |

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a **Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 _____
 (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 _____
 3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY AND STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee
☐ Publication Fee (No small entity discount permitted)
☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

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 Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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EXAMINER

KAM, CHIH MIN

ART UNIT

PAPER NUMBER

1656

DATE MAILED: 03/31/2009

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability**Application No.**

10/567,422

Applicant(s)

SCHWARTS BURD ET AL.

Examiner

CHIH-MIN KAM

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 2/9/09.
2. ☒ The allowed claim(s) is/are 1,3-12,15-20 and 46.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
(b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413),
Paper No./Mail Date _____
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/Chih-Min Kam/
Primary Examiner, Art Unit 1656

DETAILED ACTION

Status of the Claims

1. Claims 1, 3-12, 15-20 and 46 are pending.

Applicants' amendment filed February 9, 2009 is acknowledged. Applicants' response has been fully considered. Claim 1 has been amended, and claim 2 have been cancelled. Thus, claims 1, 3-12, 15-20 and 46 are examined.

Withdrawn Claim Rejections - 35 USC § 112

2. The previous rejection of claims 1-12, 15-20 and 46 under 35 U.S.C. 112, first paragraph, written description, is withdrawn in view of applicants' amendment of the claims, applicants' cancellation of the claims, and applicants' response at page 5 of the amendment filed February 9, 2009.

Examiner's Amendment

An **Examiner's Amendment** to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Leena H. Karttunen on March 16, 2009.

Examiner's Amendment to the Specification:

Please replace the term "Table 3" at page 31, line 4 with the term "Table 1".

Please replace the term "Table 4" at page 31, line 19 with the term "Table 2".

Please replace the term "Table 4" at page 32, lines 1-2 and 3 with the term "Table 2".

Please replace the term "Table 6" at page 33, line 15 with the term "Table 3".

Please replace the term "Table 7" at page 34, line 14 with the term "Table 4".

Please replace the term "Table 1" at page 37, lines 3 and 5 with the term "Table 5".

Examiner's Amendment to the Claims:

Claims 1, 3-12, 15-20 and 46 have been amended as follows:

1. (Currently amended) A method for purifying or capturing a non-immunoglobulin protein of interest having between one and ten immunoglobulin-like (Ig-like) domains from a biological fluid, comprising the steps of:

a) contacting the biological fluid containing the protein of interest with ~~an~~ a Hydrophobic Charge Induction Chromatography (HCIC) resin, wherein the HCIC resin comprises a mercapto-ethyl pyridine ligand,

b) washing out the resin with a buffer to remove unbound contaminants, and

c) eluting the protein of interest by treating the resin ~~with a solution having an acidic pH~~ or with a buffer solution comprising an organic solvent, wherein the organic solvent is isopropyl alcohol, propylene glycol and/or polyalcohols.

3. (Currently amended) ~~A~~ The method according to claims 1, wherein the organic solvent used in step c) is propylene glycol.

4. (Currently amended) ~~A~~ The method according to claim 3, wherein the concentration of propylene glycol in the solution is between about 25 and 50%.

5. (Currently amended) ~~A~~ The method according to claim 1, wherein step a) is carried out at acidic pH.

6. (Currently amended) ~~A~~ The method according to claim 5, wherein the pH used is between about 3 and 6.8.

7. (Currently amended) ~~A~~ The method according to claim 1, wherein the washing of step b) is carried out with a buffer solution having an acidic pH.

8. (Currently amended) ~~A~~ The method according to claim 7, wherein the pH used is between about 3 and 6.8.

9. (Currently amended) ~~A~~ The method according to claim 1, wherein the biological fluid is selected from a cell-conditioned culture medium, cell lysate, cell extract, tissue extract,

blood plasma, serum, milk, urine, ascites, cerebrospinal fluid, vegetable juice, plant extracts or a fraction obtained from an earlier chromatographic separation step.

10. (Currently amended) A The method according to claim 1, wherein the protein of interest has 1 to 7 Ig-like domains.

11. (Currently amended) A The method according to claim 1, wherein the protein of interest is selected from IL-18 binding protein (IL-18BP), NCAM, Fibronectin type III, ICAM-1, mad CAM-1, PE CAM- 1, VCAM-1, titin, cadherin, neurocan, LIFR, CNTFR, IL-1R, IL-3R, IL5R, IL-6R, IL- 12R, GM-CSFR, oncostatin M receptor (OSMR), VEGF receptor, FGF receptor, hPDGF receptor, T cell receptor, MHC proteins, microglobulin- β , CTLA4, B7 ~~molecule activation agent~~, neuregulin, coagulation factor XIII, ~~NF-kB~~ NF-kB, IL6-IL6R, beta-galactosidase and superoxide dismutase or an isoform, mutein, fused protein, or fragment thereof comprising at least one Ig-like domain.

12. (Currently amended) A The method according to claim 11, wherein the protein is IL-18 binding protein (IL-18BP).

15. (Currently amended) A The method according to claim 1, wherein the purification factor of the eluted protein is in the range of 11 and 94 fold.

16. (Currently amended) A The method according to claim 15, wherein the purification factor of the eluted protein is 94 fold.

17. (Currently amended) A The method according to claim 1, wherein the concentration factor of the eluted protein is in the range of 1.5 and 3.1 fold.

18. (Currently amended) A The method according to claim 17, wherein the concentration factor of the eluted protein is 3.1 fold.

19. (Currently amended) A The method according to claim 1, wherein the yield of the eluted protein is in the range of 73 and 98%,

20. (Currently amended) A The method according to claim 19, wherein the yield of the eluted protein is about 85%.

46. (Currently amended) A The method according to claim 1, wherein the purification factor of the eluted protein is in about 94 fold.

The following is an Examiner's Statement of Reasons for Allowance: The following references are closest art for the claimed invention. Schwartz *et al.* (J. Chromatography A 908, 251-263 (2001)) and Boschetti (Trends in Biotechnology 20, 333-337 (2002)) teach the use of hydrophobic charge induction chromatography (HCIC) to purify antibodies, where the antibodies bound to the resin under neutral or slightly basic condition due to hydrophobic interaction, and then were eluted out under acidic condition (e.g., pH 4.0); Burton *et al.* (J. Chromatography A 814, 71-81 (1998)) teach the use of HCIC to purify chymosin, chymotrypsinogen and lysozyme; and Weatherly *et al.* (J. Chromatography A 952, 99-110 (2002)) teach the use of HCIC to purify botulinum neurotoxin fragments. However, these references do not teach or suggest the use of HCIC to purify a non-immunoglobulin protein having between one and ten immunoglobulin-like (Ig-like) domains, where the non-immunoglobulin protein was eluted with a buffer containing an organic solvent of isopropyl alcohol, propylene glycol and/or polyalcohol. Therefore, the claims are allowable over the art of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Application/Control Number: 10/567,422

Page 6

Art Unit: 1656

/Chih-Min Kam/

Primary Examiner, Art Unit 1656

CMK

March 16, 2009